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FDA

AND THE VETERINARIAN



U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
Center for Veterinary Medicine
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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

To the veterinarian:

The Food and Drug Administration (FDA) is responsible for ensuring that animal drugs are safe and effective for their intended use and that food from treated animals is safe for human consumption. Veterinarians use and dispense drugs for the prevention and treatment of diseases in animals. While FDA does not regulate the practice of medicine, regulations established to carry out mandated responsibilities related to the use of drugs in animals, especially food animals, do preclude some options.

This booklet, prepared by the Center for Veterinary Medicine, is intended to provide you with a concise summary of the enforcement activities of the Agency as they relate to the use of animal drugs.

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INTRODUCTION

The FDA has the broad mandate to assure the safety and effectiveness of drugs (including animal drugs and their use) and the safety of the food supply. This responsibility is derived from the Federal Food, Drug, and Cosmetic Act (the Act). The Act was amended in 1968 to include sections which specifically address animal drugs. It was the intent of these amendments to consolidate and revise the Act to ensure that animal drugs are safe and effective for their intended uses and that they do not result in unsafe residues in foods from treated animals.

Section 512 of the Act, the basic statutory provision governing new animal drugs, provides that a new animal drug shall be deemed unsafe unless there is in effect an approval of a new animal drug application and that the intended use of a drug and its labeling must conform to the approved application. A drug which does not conform to the provisions of section 512 is deemed adulterated and is subject to the enforcement provisions of the Act. Virtually all animal drugs are "new animal drugs" within the meaning of the term in the Act, and so are subject to section 512. Although an animal drug may avoid the approval requirement if it is not a new animal drug or is grandfathered, the burden is on the marketer to prove that one of these exceptions applies.

To assist in carrying out its statutory responsibilities, the FDA has promulgated regulations and developed written regulatory policies. New regulations are published in the *Federal Register*.¹ All FDA regulations are codified in Title 21 of the Code of Federal Regulations.² These regulations and policies are subject to change as new circumstances occur and new information becomes available. Because they are always subject to legal challenge, they must be scientifically and legally defensible.

Most regulatory issues can be adequately and appropriately resolved through dialogue in various forms. The FDA encourages such open, frank discussions.

¹The *Federal Register* serves as a legal newspaper for making available to the public regulations and legal notices issued by Federal agencies. It is published Monday through Friday by the Office of the Federal Register, National Archives and Records Administration, Washington, D.C. 20408. Distribution is made only by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

²Available from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402.

WHO HAS RESPONSIBILITY?

While the Food and Drug Administration is responsible for regulating animal feeds/foods and most animal health products, there are some classes of animal products that fall under the jurisdiction of other Federal agencies. A quick guide as to which agency has responsibility for these products is provided below.

Pet Foods

Pet foods are subject to the requirements of the Act, and pet food manufacturers are subject to individual annual product registration in most states. State laws may require that pet food labels bear, in addition to the mandatory information required by Federal law, a label statement of "guaranteed analysis" for minimum protein and fat content, maximum fiber content and, in some instances, maximum moisture content. Additional information concerning state registration and labeling requirements may be obtained from the individual states where the products will be distributed or from the *Official Publication of the Association of American Feed Control Officials, Inc.* c/o West Virginia Department of Agriculture, Capitol Complex/Guthrie Center, Charleston, West Virginia, 25305.

Pet foods are also subject to the labeling requirements of the Fair Packaging and Labeling Act, which governs certain aspects of consumer product labeling.

As with human food, pet foods may not be adulterated or misbranded. Pet foods may not contain any poisonous or deleterious substances or residues of pesticides in excess of established tolerances. They may not be stored in any containers which may render the contents injurious to health because of any poisonous or deleterious substance and may not contain any color additives or food additives which are unsafe. To ensure safety, canned pet food must be manufactured and registered in accordance with the FDA regulations for low-acid canned foods. Pet food labeling may not be false or misleading in any particular. Damage or inferiority may not be concealed in any manner. Pet food may not be sold under the name of any other food and may not have any valuable constituents omitted or extracted.

Animal Biologics

The term animal biologics includes all viruses, serums, toxins, and analogous products of natural or synthetic origin, such as diagnostics, antitoxins, vaccines, and the antigenic or immunizing components of microorganisms intended for use in the diagnosis, treatment, or prevention of disease in animals. The Veterinary Biologics Staff, Animal and Plant Health Inspection Service, U.S. Department of Agriculture is responsible for regulating

veterinary biologics for purity, safety, potency and effectiveness.

Pesticides

Gennicidal preparations for use on inanimate objects, as well as rodenticides, and most insecticides are subject to the Federal Insecticide, Fungicide, and Rodenticide Act, administered by the Pesticide Regulation Division of the Environmental Protection Agency (EPA), Washington, D.C. 20460. However, some products used to control external pests are intended to act systemically and, therefore, are regulated as drugs by the FDA and not as pesticides by the EPA. For example, topically applied flea control products are usually regulated by EPA, whereas orally administered flea control

products generally fall under FDA's jurisdiction. In those situations where violative residues of pesticides are detected in animal-derived human food products, FDA has the responsibility for regulatory enforcement.

Animal Grooming Aids

The animal counterpart of a cosmetic is commonly referred to as a "grooming aid." The Act defines a cosmetic as pertaining only to human use (201(i)). Therefore, products intended for cleansing or promoting attractiveness of animals are not subject to FDA control. However, if such products are represented for any therapeutic purpose or if they contain an active drug ingredient they are subject to the Act as animal drugs.

THE DRUG APPROVAL PROCESS

Under the Federal Food, Drug, and Cosmetic Act, the term "drugs" means articles recognized in the official United States Pharmacopeia, official Homeopathic Pharmacopeia of the United States, or official National Formulary; articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and articles other than food intended to affect the structure or any function of the body of man or other animals. It also includes articles

intended for use as a component of a drug.

Once a product is determined to be a drug, the next step is to determine whether or not it is a new animal drug. The Act defines a new animal drug (in part) as any drug intended for use for animals other than man, the composition of which is not generally recognized, among experts qualified by scientific training and experience, as safe and effective for use under the conditions prescribed, recommended,

or suggested in its labeling.

Before a new animal drug may receive formal FDA approval, it must be established by scientific testing as effective and safe by the sponsor of the drug product. If the product is intended for use in a food-producing animal, it must also be established as safe for humans, and the data must show that the edible animal products are free of unsafe residues. The sponsor must also develop analytical methods to detect and measure drug residues in edible animal products. It is the responsibility of the drug sponsor (individual or firm seeking FDA approval of the drug product) to conduct the necessary tests.

The sponsor may select outside investigators to conduct clinical trials of the drug as long as they are qualified by scientific training and experience, and agree to comply with the investigational protocol and all applicable regulations. FDA has established regulations for non-clinical investigations, such as toxicology studies, and regulations and guidelines for conducting and monitoring clinical trials.

When the sponsors believe that sufficient data have been collected to establish the safety and effectiveness of their drug product, they may apply for approval. A New Animal Drug Application (NADA) is submitted along with supporting data, including all adverse effects associated with the drug's use. The NADA must also include information on the drug's chemistry; composition and component ingredients; manufacturing methods, facilities, and

controls; proposed labeling; analytical methods for residue detection and analysis if applicable; environmental impact assessment; and other information.

The FDA review of the NADA submitted by drug sponsors is very detailed and comprehensive. Initially, FDA scientists will determine whether the data have been developed in accordance with Good Laboratory Practice Regulations and the clinical trial guidelines. If the studies were conducted properly, the data are then evaluated with respect to drug safety and effectiveness.

The animal safety data for a drug product must relate to the dosage level and route of administration proposed in the labeling. The primary objective is to determine the safety of the product relative to labeled usage. Examples of some questions that must be answered concerning the safety of the drug product to the animal are:

- (1) What is the toxicity in the target animal?
- (2) Is the product a teratogen, carcinogen, or mutagen?
- (3) What is the margin of safety?
- (4) Are observed toxic effects (if any) reversible?
- (5) Does the product affect reproduction?

At the conclusion of the animal safety review, a summary is prepared which explains why the product is safe or not shown to be safe. If the product has been shown to be safe, any restrictions or constraints on use must be enumerated. All warning and caution statements to

be placed on the label must be enumerated and included in the summary, as well as any expected side effects.

All effectiveness data submitted must relate either directly or indirectly to the specific label and labeling claims made for the product. Basically, the petitioner must demonstrate that the product produces the claimed effect. As a minimum, the data must have four basic attributes:

- (1) The data must come from adequate and well-controlled studies.
- (2) The data must demonstrate that the dose response relationship has been established.
- (3) The studies must have been performed in several locations so that any geographic or environmental effects can be evaluated.
- (4) The major portion of the data must come from studies in which the proposed label dosage and route of administration were used.

Since no drug is absolutely safe or

totally effective, approval of a drug product from a target species standpoint must rest on an assessment of the degree of acceptable risk when weighed against the potential therapeutic benefit. Such risk/benefit weighing is not done with respect to human food safety.

Development of adequate methods for detecting drug residues and their metabolites is frequently the most time-consuming and expensive item in developing a new animal drug for food-producing animals. Methods may have to be developed for muscle, liver, kidney, fat, milk, and/or eggs sensitive to levels that assure food safety. The proposed residue methodology must be validated prior to approval of the NADA and must show satisfactory performance in one USDA and two FDA laboratories. If the method proves to be practical, of sufficient sensitivity, and is validated in the three laboratories, FDA will approve the method.

When an NADA is deemed approvable, a regulation is published in the *Federal Register* announcing its approval and is incorporated into the Code of Federal Regulations.

CLASSIFYING Rx AND OTC ANIMAL DRUGS

FDA has the responsibility for determining the marketing status (prescription or over-the-counter) of animal drug products based on whether or not it is possible to prepare "adequate directions for use" under which a layperson

can use the drugs safely and effectively. Products for which adequate directions for lay use can be written must be labeled for over-the-counter (OTC) use under existing law. If adequate directions cannot be written, the prescription

(Rx) system provides a method of distribution and control which is intended to assure that the Rx product reaches only the hands of persons trained to use the product. This can include, in addition to the veterinarian, animal owners or managers who the veterinarian has determined are capable of using the product safely under the practitioner's supervision.

Safe use includes safety to the animal, safety of food products derived from the animal, safety to the person administering the drug, safety to persons associated with the animal, and safety in terms of the drug's impact on the environment.

Effective use of a drug product

assumes that an accurate diagnosis can be made with a reasonable degree of certainty that the drug can be properly administered, and that the course of the disease can be followed so that the success or lack of success of the product can be observed.

The same drug substances can be marketed in a number of different dosage forms, intended for use by varying routes of administration, and in varying species of animals. Thus, these drug products may be appropriately labeled Rx in some cases and OTC in others.

Rx products must bear the legend: "Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian."

DISPENSING VETERINARY PRESCRIPTION DRUGS

Since adequate directions for safe and effective lay use cannot be written for veterinary prescription drug products, such products can only be sold to or on the prescription or other order of a licensed veterinarian. Prior to being sold or dispensed, they must remain in the possession of a person or firm regularly and lawfully engaged in the manufacture, transportation, storage, or wholesale or retail distribution of veterinary prescription drug products. The drug products may be distributed only by persons or firms authorized by state and local laws.

Sale (dispensing, shipping, or otherwise making available for use in animals)

to the layperson of a veterinary prescription drug product may be made only by or on the bona fide prescription or other order of a licensed veterinarian. The FDA has interpreted the word "prescription" to apply only to the practitioner's direction to a pharmacist. Because some states authorize persons other than pharmacists to dispense prescription drug products on a veterinarian's instructions the term "other order" is used when instructions are for a legally authorized dispenser who is not a pharmacist. In both cases the instructions and their intent are the same and the dispenser may not dispense an Rx drug product without a

veterinarian's explicit authorization.

Sale of a veterinary prescription legend drug product to a layperson, except on a prescription or on order of a licensed practitioner, causes the product to be misbranded since it fails to bear adequate directions for lay use and does not meet all the requirements of the exemption, and subjects the seller to civil and/or criminal provisions of the Act.

A licensed veterinarian may legally use or dispense a veterinary prescription drug product only within the course of his/her professional practice where a valid veterinarian-client-patient relationship exists. Veterinarians employed by drug manufacturers or distributors may not legally dispense prescription drug products to laypersons unless they meet the above criteria. Similarly, practicing veterinarians or their employees may not legally sell veterinary prescription drug products to walk-in customers unless the same criteria are met.

Federal regulations require that drug manufacturers provide at least the following information on the label of the finished package form of veterinary prescription drug products:

- (1) the statement, "Caution:
Federal law restricts this drug to use by or on the order of a licensed veterinarian";
- (2) recommended or usual dosage;

- (3) the route of administration, if it is not for oral use;
- (4) the quantity or proportion of each active ingredient;
- (5) the names of inactive ingredients if it is for other than oral use;
- (6) an identifying lot or control number;
- (7) manufacturer's or distributor's name and address; and
- (8) net quantity contents.

When issuing a prescription or other order, the veterinarian must inform the dispenser as to the information to be placed on the labeling of the dispensed product which must include at a minimum the information listed below:

- (1) name and address of the veterinarian who prescribed or ordered the drug product;
- (2) directions for use; and
- (3) any necessary cautionary statements including withdrawal times.

Any additional requirements of state or local laws for dispensed veterinary drug products must also be followed.

To protect themselves and their clients, veterinarians should make efforts to ensure their instructions are followed, especially when they prescribe or recommend drugs for food-producing animals that require a withdrawal period.

DRUGS IN ANIMAL FEEDS (Medicated Feeds)

Anyone who adds drugs to feed is subject to the Federal Food, Drug, and Cosmetic Act. Just as each label claim for a new animal drug must be approved, so too must the drug be specifically approved for administration in animal feed. Approvals are issued only for uses, claims and drug levels which have been shown to be safe and effective by adequate and well-controlled studies. Also, the feed has to be labeled in accordance with the regulations if sold or delivered to a second party.

Veterinarians (whether practicing or employed by a feed manufacturer) may only direct a drug to be mixed into feed

for uses and at potency levels specifically permitted by the regulations in 21 CFR Part 558. The person or firm mixing a medicated feed must be registered with the FDA as a drug manufacturer and hold a medicated feed application (Form FDA 1900) unless exempted by regulation from registering and obtaining such approval.

If a drug has been added to animal feed for uses or at levels not specified in the regulations, a violation of the Act has occurred. Any individual authorizing the violation as well as the individual illegally mixing the feed may be subject to regulatory action. Additionally, the feed itself may be subject to seizure.

VETERINARY DEVICES

By statutory definition, a medical device is an instrument, apparatus, implement, machine, contrivance, implant, *in vitro* reagent, or other similar or related article, including any component part, or accessory, which is intended for use in the diagnosis of disease, or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or intended to affect the structure or any function of the body of man or other animals and which does not achieve any of its principal intended purposes through chemical action within or on the body of man or other animals and which is not

dependent upon being metabolized for the achievement of any of its principal intended purposes.

Veterinary medical devices and diagnostic aids are subject to the general provisions of the Act in regard to misbranding and adulteration. There are currently no requirements for FDA pre-market approval of devices intended for animal use. However, animal device labeling may not be false or misleading under the existing Act. A veterinary medical device may be considered misbranded if the manufacturer or distributor does not have data which establish the safety and effectiveness of

the claims made for the product. Devices are illegal if dangerous to animal or human health when used in the manner prescribed, recommended, or suggested in labeling. The FDA relies on veterinarians and other users to report unsafe devices.

If adequate directions cannot be written for lay use, the device is deemed unsafe for use except under the supervision of a licensed veterinarian.

The FDA, therefore, requires that the label bear the statement: "Caution: Federal law restricts this device to sale by or on the order of a licensed veterinarian" (21 CFR 801.109). Examples of veterinary medical devices which are required to bear the prescription legend include transcutaneous electronic nerve stimulators, pulse magnetic field devices, and lasers.

RESPONSIBILITY FOR ILLEGAL RESIDUES IN MEAT, MILK, AND EGGS

FDA is responsible for programs and regulatory actions aimed at preventing illegal drug residues in human food products from treated animals. Illegal drug residues in edible products can constitute a hazard to the health of persons consuming such food. Failure to observe label withdrawal periods before slaughter or failure to withhold milk is the principal cause of illegal drug residues. Other causes may include failure

to follow other label directions, poor feed manufacturing practices, and human negligence. Regardless of the cause, it is FDA's policy to hold responsible any individual in the production and marketing chain who can be shown to have caused (by an act of commission or omission) illegal residues in edible animal products. If justified by the facts, legal charges will be considered against these individuals.

EXTRA-LABEL USE OF NEW ANIMAL DRUGS IN FOOD-PRODUCING ANIMALS

"Extra-label use" refers to the actual or intended use of a new animal drug in a food-producing animal in a manner that is not in accordance with the approved drug labeling. This includes, but is not limited to, use in species or for indications not listed in the labeling, or use at dosage levels other than those stated in the labeling. The Act itself provides no special exemption

for the manner in which veterinarians use drugs in their practices. If a new animal drug is used for an unlabeled purpose, it may be deemed unsafe under Section 512 (a)(1)(B) and in violation.

FDA recognizes that there are some diseases in some species for which no drugs are approved and a strict enforcement policy would preclude the veterinarian's ability to treat these conditions.

The Agency also recognizes that when a drug product is used extra-labelly there are inadequate data to demonstrate the safety of food products derived from the treated animal. For example, data on adequate withdrawal times, the toxicological significance of residues of the parent compound and/or its metabolites, and, frequently, an analytical method to detect the presence of any residues may all be lacking. The FDA has adopted an extra-label drug use policy which describes the Agency's enforcement priorities and which is intended to provide rational options for the veterinarian to consider where undue suffering or death might otherwise occur. The policy is also intended to protect the public health under these circumstances.

Under the current policy, extra-label drug use is a responsibility veterinarians (and only veterinarians) may assume when treating food-producing animals under conditions when the health of animals is immediately threatened and suffering and/or death would result from failure to treat the affected animals in an extra-label manner. In instances of this nature, regulatory action would not ordinarily be initiated provided the following criteria are met and precautions observed:

- (1) A careful medical diagnosis is made by an attending veterinarian within the context of a valid veterinarian-client-patient relationship;³
- (2) A determination is made that
 - (a) there is no marketed drug specifically labeled to treat the

condition diagnosed, or (b) drug therapy at the dosage recommended by the labeling has been found clinically ineffective in the animals to be treated;

- (3) Procedures are instituted to assure that identity of the treated animals is carefully maintained; and
- (4) A significantly extended time period is assigned for drug withdrawal prior to marketing meat, milk, or eggs; steps are taken to assure that the assigned timeframes are met and no illegal residues occur.

³ A valid veterinarian-client-patient relationship has been described by the American Veterinary Medical Association as follows:

An appropriate veterinarian-client-patient relationship will exist when:

- (1) the veterinarian has assumed the responsibility for making medical judgements regarding the health of the animal(s) and the need for medical treatment, and the client (owner or other caretaker) has agreed to follow the instructions of the veterinarian; and when (2) there is sufficient knowledge of the animal(s) by the veterinarian to initiate at least a general or preliminary diagnosis of the medical condition of the animal(s). This means that the veterinarian has recently seen and is personally acquainted with the keeping and care of the animal(s) by virtue of an examination of the animal(s), and/or by medically appropriate and timely visits to the premises where the animal(s) are kept; and when (3) the practicing veterinarian is readily available for follow-up in case of adverse reactions or failure of the regimen of therapy.

Therefore, extra-label use of drugs in treating food-producing animals may, under this policy, be considered only in special circumstances. The "exempting" criteria do not include drug use in treating food-producing animals by the layperson. Laypersons are generally not expected to have sufficient knowledge and understanding concerning animal diseases, pharmacology, toxicology, drug interactions, and other scientific parameters to use drugs in treating food-producing animals in any way other than as labeled.

Certain drugs may not be used in treating food-producing animals even under the cited criteria. These include diethylstilbestrol and chloramphenicol. Extra-label uses of drugs in treating food-producing animals for improving rate of weight gain, feed efficiency, or other production purposes, or for routine disease prevention, are inappropriate, as is use for therapeutic purposes other than under the circumstances described

above. The criteria cited above do not sanction the sale and use, for any purpose, of new animal drugs that are not approved. Nor may a drug (including a bulk drug) be mixed into feed for any use or at a potency level not specifically permitted by the regulations in 21 CFR Part 558, even if prescribed or ordered by a veterinarian. Furthermore, a finding of illegal drug residues is not a prerequisite for initiating regulatory action based on extra-label drug use in food-producing animals.

Finally, FDA will not ordinarily recommend regulatory action in the case of extra-label use by veterinarians treating non-food animals except in cases where there is a clear threat to the public health or the health and welfare of the animal is threatened, or if other serious consequences occur. This regulatory discretion is based upon the presumption of a bona fide veterinary-client-patient relationship.

BULK NEW ANIMAL DRUG SUBSTANCES

Bulk new animal drugs (sometimes called bulk drugs or chemicals) are new animal drug substances intended for use in the compounding of a finished dosage form new animal drug product. The importation or domestic purchase of bulk new animal drug substances by veterinarians (or anyone else) for compounding prescriptions in their private practice is illegal unless the individual has an approved NADA or an Investigational New Animal Drug (INAD) exemption for clinical investigation. Bulk

new animal drug substances for which there are no approved NADA or INAD exemptions are considered to be misbranded and/or adulterated under the Federal Food, Drug, and Cosmetic Act. The Act does permit compounding for use within a professional practice if the finished product is not a new animal drug or is "grandfathered" under the Act.

Bulk new animal drug substances labeled for further manufacturing or processing that bear label indications

for veterinary use and bulk certifiable antibiotics are by law adulterated. They are unapproved new animal drugs unless the recipient or distributor holds an approved NADA or an INAD exemption for preparation of a finished dosage form drug or medicated feed from that particular bulk drug source.

Bulk drug substances labeled for further manufacturing or processing, which do not bear label indications for veterinary use, may be misbranded under the Act if an intention for veterinary use is established and the distributor does not establish that the intended finished product is approved by FDA or is exempt from the approval requirement. Such drugs are in violation because they do not bear adequate directions for veterinary drug use and they are not exempt from adequate directions for use.

REPORTING ADVERSE DRUG REACTIONS

Sponsors of approved new animal drug products are responsible for establishing and maintaining records concerning experiences with the drugs and for submitting reports of those experiences to FDA. Among the data which must be submitted are reports of injury, toxicity, sensitivity reaction, unexpected incidence or severity of side-effects associated with use or failure of the drug to exhibit expected pharmacological action. FDA scientists analyze this data to determine if any modifications are needed in the drug's labeling, dosage level, etc., to prevent future adverse reactions. In

New animal drug substances may be imported or purchased domestically only if the individual is:

- (1) the holder of an approved NADA for the new animal drug substance; or,
- (2) the sponsor or investigator named in an INAD exemption for the drug substance for clinical investigation; or
- (3) the investigator conducting tests *in vitro* and in laboratory research animals with drugs which comply with pertinent Federal regulations; or
- (4) a distributor holding the requisite approvals or having an order from a consignee holding the approved NADA or INAD exemption.

extreme instances, the adverse reactions may be so severe as to require withdrawal of approval of the drug. However, because of the extensive premarketing approval process, this rarely occurs.

FDA also encourages reporting of adverse drug reactions by veterinarians. The reports should be submitted on Form FDA 1932a, "Veterinary Alert to Adverse Reaction." This is a pre-addressed, postage-paid form which is filled out and dropped in the mail by the veterinarian. Copies of the form are usually available from state veterinary medical associations, clinics of colleges of veterinary medicine,

USDA Extension Service veterinarians, and FDA offices. FDA may occasionally need more detailed information about an incident, and the veterinarian may be called by a FDA staff veterinarian. In any event all forms are acknowledged by letter and another form is sent for future use.

Adverse reactions may be reported by

telephone during normal working hours (7:00 a.m. to 4:00 p.m. Eastern Standard/Daylight Time) by calling collect 301-443-4095, or after hours by dialing direct 301-443-1209. In the second case a message is recorded and your call is returned by a veterinarian the following working day.

INTERACTION WITH THE FOOD AND DRUG ADMINISTRATION

The Food and Drug Administration is most effective in carrying out its mission under a policy of openness and free communication. All parties are best served when there is clear understanding of the FDA's regulations and policies and how they are administered. By operating under this policy, FDA hopes to create confidence in, and support for, programs that are intended to promote and protect the health and well being of all.

FDA encourages anyone to contact the Agency for assistance, to supply information, or to report a problem with a product. To help direct requests to the proper location for a rapid response, we offer the following guidance:

- To obtain information on approved drugs, regulations, policies, or to submit suggestions or comments, address your letter to:

Food and Drug Administration
Center for Veterinary Medicine
5600 Fishers Lane
Rockville, Maryland 20857

- To request copies of a specific FDA document:

Food and Drug Administration
Freedom of Information Staff,
HFI-35

5600 Fishers Lane
Rockville, Maryland 20857

- To report an adverse drug reaction:
Call Collect: 301-443-4095 from 7:00 a.m. - 4:00 p.m. Eastern Standard (or Daylight) Time, Monday- Friday. After hours call 301-443-1209 (not a collect call) to leave a message and your call will be returned by a veterinarian the next working day.
- To report a violation of the Federal Food, Drug, and Cosmetic Act:
Contact your nearest FDA office or
Division of Compliance
(HFV-230)
Center for Veterinary Medicine
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857
Telephone: 301-443-3336

TYPES OF FDA REGULATORY ACTIONS

The objective of FDA regulatory programs is to assure compliance with the Federal Food, Drug, and Cosmetic Act. Specific enforcement activities include actions to correct and prevent violations, remove violative products or goods from the market, and punish offenders. The type of enforcement varies with the nature of the violation. These range from a letter notifying the individual or firm of a violation and requesting correction to criminal prosecution of the individual or firm. Findings of adulteration or misbranding usually lead to an individual who failed to take steps to assure compliance with the law. Such individuals can be charged as violators and if guilty are subject to the penalties specified by the law.

Regulatory letters and notice of adverse findings letters are sent to the individuals, advising them of specific noted violations. These letters require a written response as to the steps which will be taken to correct the violation. These letters constitute two forms of non-compliance warnings that can be issued under current Agency policy.

Criminal prosecution may be recommended where:

- (1) there is a clear and substantial violation;
- (2) there is sufficient evidence to warrant the belief that a trial would find the defendants to be guilty; and

- (3) it is reasonable and just to impose the criminal process.

Under current FDA policy, criminal prosecution is usually preceded by warning to the firm or individual(s) involved.

Seizure - An action brought under admiralty proceedings against an animal feed, drug, or device which is in violation of the Federal Food, Drug, and Cosmetic Act for being adulterated and/or misbranded. The purpose is to remove a specific lot of goods from the channels of commerce.

Injunction - A writ granted by a court whereby one is required to do or refrain from doing a specific act. In most instances FDA seeks injunctions against individuals and/or corporations to prevent them from violating or causing violations of the Federal Food, Drug, and Cosmetic Act.

The FDA field offices have primary responsibility for initiating and recommending regulatory action. The type of action recommended will depend upon the nature of the violation and the public health concern, Agency policy, previous history of violations by the firm, and other factors. FDA headquarters offices approve enforcement actions. Approved recommendations for criminal prosecution and injunction are transmitted to the Justice Department; approved seizure recommendations are sent to the appropriate United States attorney for filing in Federal court.

FINES FOR FD&C ACT VIOLATIONS

Misdemeanor fines under the Food, Drug, and Cosmetic Act have been increased so that the maximum fine, formerly \$1,000 per count, may now reach \$500,000 under some circumstances.

The increase is a result of the Criminal Fine Enforcement Act of 1984 (Public Law 98-596) that provides new fines for Federal law violations perpetrated after Jan. 1, 1985. Although the act is an amendment to the criminal statutes, not the FD&C Act, the Justice Department has advised FDA that it applies to the fines levied under the FD&C Act, other statutes that contain provisions enforced by FDA, and to all Federal crimes in Federal law.

The following fines are applicable for each offense:

- Up to \$100,000 for a misdemeanor by a corporation or individual that does not result in death.
- Up to \$250,000 for a misdemeanor by an individual that results in death, or for a felony.
- Up to \$500,000 for a misdemeanor by a corporation that results in death, or for a felony.

The maximum imprisonment for a misdemeanor under the FD&C Act remains a year for each offense.

GLOSSARY

Adulteration - A violation of the Federal Food, Drug, and Cosmetic Act which includes products that are defective, unsafe, filthy, or produced under insanitary conditions. It also includes products which are manufactured under procedures and controls which do not comply with Current Good Manufacturing Practice regulations as well as new animal drug products which are not the subject of an NADA approval. Detailed definitions of adulteration are in the Act itself, and have been developed in regulations and by the courts.

Adverse Drug Reaction - An unexpected side effect, injury, toxicity, sensitivity reaction, or unexpected incidence or severity of side effects associated with use of a new animal drug product. The failure of a new animal drug product to exhibit expected pharmacological action also is an adverse drug reaction.

Animal Feed - An article which is intended for use as a substantial source of nutrients in the diet of the animal. It is not limited to a mixture intended to be the sole ration of the animal.

Device - An instrument, apparatus, implement, machine, contrivance, implant, *in vitro* reagent, or other similar or related article, including any component part or accessory, which is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or intended to affect the structure or any function of the

body of man or other animals, and which does not achieve any of its principal intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its principal intended purposes.

Drug - An article (1) recognized in the official United States Pharmacopeia, official Homeopathic Pharmacopeia of the United States, or official National Formulary, or any supplement to any of them; (2) intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; (3) intended to affect the structure or any function of the body of man or other animals; and (4) intended for use as a component of any articles specified in clause (1), (2), or (3); but does not include devices or their components, parts, or accessories.

Extra-Label Use - Refers to the actual or intended use of a new animal drug in a manner that is not in accordance with the approved label directions.

Injunction - A writ granted by a court whereby one is required to do or refrain from doing a specific act. In most instances FDA seeks injunctions against individuals and/or corporations to prevent them from violating or causing violations of the Federal Food, Drug, and Cosmetic Act.

Investigational New Animal Drug (INAD) - Statutory authority to exempt new animal drugs from the requirements of an approved new animal drug application is found in Section 512 (j) of the Federal Food, Drug, and Cosmetic Act. This exemption specifically limits the distribution of unapproved new animal drugs only for use by experts, qualified by scientific training and experience, to investigate the safety and effectiveness of animal drugs. In order to distribute a new animal drug for clinical investigations, an exemption from the requirements of an approved new animal drug application must be claimed. This is accomplished by the submission of certain information referred to as an INAD (Investigational New Animal Drug) application.

Labeling - All labels and other written, printed, or graphic matter (1) upon any article or any of its containers or wrappers or (2) accompanying such article.

Medicated Animal Feed - An article intended for use as food for animals, other than man, bearing, containing, or purporting to bear or contain any kind of animal drug/drug combination.

Medicated Feed Application (Form FDA-1900) - A new animal drug application providing for the use of new animal drugs in feed and submitted by the sponsor, manufacturer, or authorized agent.

Misbranding - A violation of the Federal Food, Drug, and Cosmetic Act which includes statements, designs, or pictures in labeling that are false or misleading, and failure to provide required information in labeling. A detailed definition of misbranding is in the Act and has been developed further in regulations and judicial decisions.

New Animal Drug - Any drug intended for use for animals other than man which, among other things, is not generally recognized by qualified experts as safe and effective for use under the condition prescribed, recommended, or suggested in the labeling thereof. Certain antibiotics, which are new animal drugs per se, are excepted.

Seizure - An action brought under admiralty proceedings against an animal feed, drug, or device which is in violation of the Federal Food, Drug, and Cosmetic Act for being adulterated and/or misbranded. The purpose is to remove a specific lot of goods from the channels of commerce.

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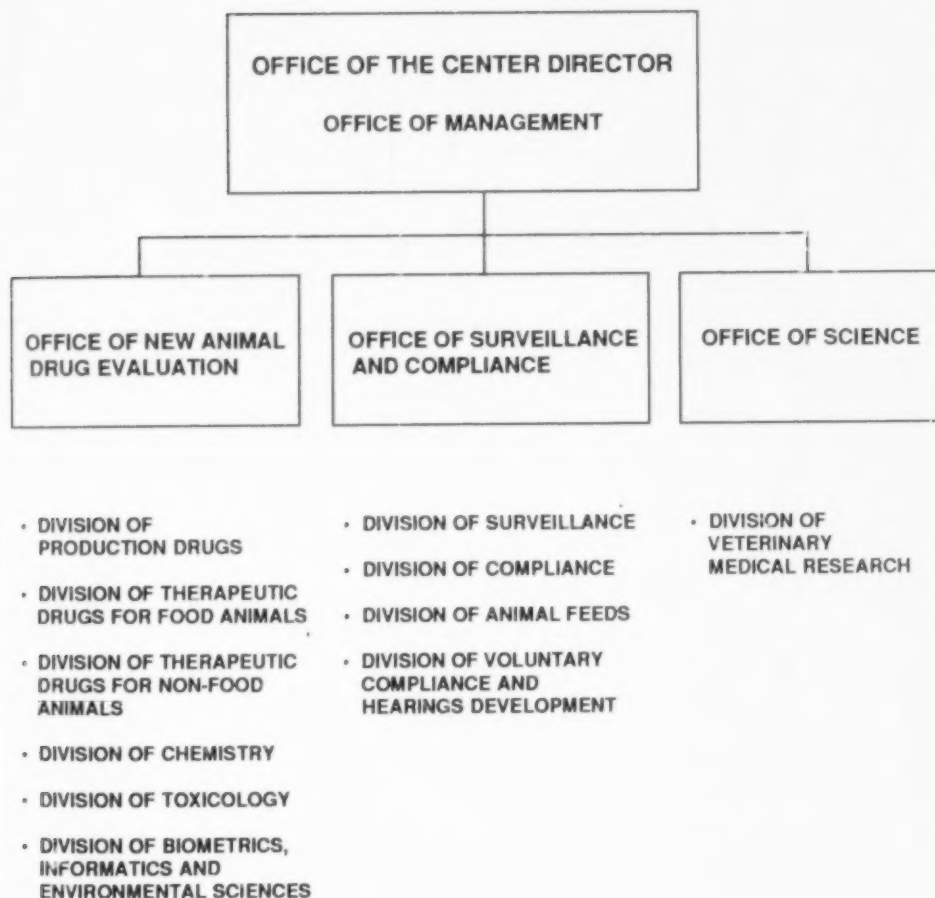
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